Institute of Molecular and Cell Biology
A*STAR

SEMINAR ANNOUNCEMENT

We would like to invite you to attend this seminar hosted by Prof Vinay Tergaonkar:

Date: 14 October 2019, Monday
Time: 11:00AM – 12:00NN
Venue: Level 3, IMCB Seminar Room 3-46, Proteos, Biopolis

Speaker: A/Prof Michael Samuel, Head, Tumour Microenvironment Laboratory, Centre for Cancer Biology, Australia
Title: How tumours co-opt ER stress signalling to remodel the tumour microenvironment

Abstract
The extra-cellular matrix (ECM) is a source of biochemical and biomechanical influences that direct cell proliferation and fate. However, the molecular mechanisms underlying the interplay between these influences and tissue homeostasis are still relatively ill-defined. The ROCK signalling pathway lies at the interface between mechanical and biochemical signalling. We have shown that ROCK signalling promotes tumour progression by increasing the production of ECM proteins such as collagen, fibronectin, periostin and tenascin C, thereby elevating ECM stiffness and enhancing integrin-mediated mechanotransduction signalling in tumours (1,2). We now have new insight into the mechanisms by which breast cancers recruit and educate tumour-promoting fibroblasts that produce a stiff ECM in a ROCK-dependent manner. We have identified a key mediator of fibroblast education downstream of ROCK. In vivo and ex vivo analyses have revealed that ROCK activity in cancer cells selectively engages the PERK unfolded protein response, resulting in the secretion of Creld2. This protein acts on fibroblasts within the microenvironment to enhance their CAF-like properties including increased production of ECM proteins, thereby accelerating tumour progression. Intriguingly, women with breast cancers exhibiting high levels of CRELD2 had a lower 5-year survival rate than women whose breast cancers produced low levels. We propose that CRELD2 is a prototypic secreted factor downstream of ROCK, that mediates a mechanoreciprocal feed-forward mechanism by educating fibroblasts, and that inhibiting such secreted effectors of ROCK may be a novel therapeutic approach to target invasive and metastatic cancers.

Biography
Michael Samuel is a cancer biologist and heads the Tumour Microenvironment Laboratory at the Centre for Cancer Biology, Adelaide. His research program focuses on elucidating the reciprocal biochemical and biomechanical signals travelling between tumours and their microenvironments to regulate tumour progression and metastatic potential. To underpin this work, he has established novel murine models of altered signalling that are used in his laboratory to dissect out key novel players in cancer-microenvironment signalling. This has helped identify several secreted factors, validated using human samples, that provide insights

into how cancers modify their microenvironments and that may be targeted to halt tumour progression and metastasis.

ALL ARE WELCOME *(No registration required)*

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